PATENT
0508-1011-1

IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of:

BARTHOLEYNS et al. Conf. 2789

Application No. 10/622,727 Group 1642

Filed: July 21, 2003 Examiner: Misook Yu

COMBINED PREPARATION FOR THE TREATMENT OF NEOPLASIC DISEASES OR OF INFECTIOUS DISEASES

DECLARATION UNDER RULE 132

Assistant Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Jacques Bartholeyns, am European project coordinator for I.D.M. Immuno-Designed Molecules of Paris, France and hereby declare as follows:

I am one of the inventors of the above-identified U.S. patent application.

I am familiar with the Examiner's position that the claimed method of treating a patient suffering from a neoplastic or infectious disease, comprising administering an effective amount of monocyte derived cells and an effective amount of chemotherapy drugs would have been obvious under 35 USC 103(a)because Bartoleyns et al. (Immunobiology 1996) disclose a method of treating cancer using monocyte derived cells and that

stimulation against a tumor might only be successful when the tumor has been reduced to manageable by prior chemotherapy. We do not believe that the publication teaches the claimed invention for the reasons set forth in the response that accompanies this declaration. Furthermore, the Official Action fails to appreciate the unexpected effects of administering an effective amount of both monocyte derived cells and chemotherapy drugs.

To show the unexpected effects, a phase I-II clinical study was completed at the Erasme University Hospital in Brussels, Belgium, on stage III or TV melanoma patients injected with monocytes derived dendritic cells. This protocol was supported by a contract BIO4—CT97-2216 from the European Commission under the Biotech programme.

Melanoma patients were included for the study after progression following surgery and chemotherapy treatments. They received 4 injections of 10 to 100 million autologous dendritic cells derived from blood monocytes and loaded with melanoma call line lysate.

All patients had advanced disease and were treated previously by surgery and different chemotherapy protocols and become refractory.

Fifteen patients were included in the study. Of the 15 patients, nine (9) received effectively the dendritic adoptive therapy. Among these patients, who were all progressive at inclusion, five progressed, two stabilized their metastatic

disease, one had a partial response and one presented a complete clinical response.

This patient was treated with melphalan chemotherapy. One month later, he was diagnosed with progressive disease and included in the study. After the third injection, the patient presented a partial clinical response, with regression of dozen of transit metastatic nodules.

After completion of the adoptive monocyte derived cell therapy, a complete clinical response was documented and the patient remained tumor free since.

This clinical case demonstrates that even patients with progressive stage IV advanced melanoma can be treated with a sequence of chemotherapy and monocytes derived dendritic vicinal therapy to achieve a significant clinical response despite the deleterious effects of chemotherapy on cells.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United

States code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Jacques Bartholeyns, PhD

Date Feb 23, 2007